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Abstract

Basophil histamine release induced by allergens (house dust and *Candida albicans*) and anti-IgE was examined in 31 patients with bronchial asthma in relation to patient age, age at onset of the disease and serum IgE levels. Basophils from patients under 40 years of age generally released a significantly large amount of histamine by stimulation with house dust and anti-IgE. On the other hand, histamine release from patients over 41 years of age was generally not marked when the cells were incubated with house dust and anti-IgE, although, in some cases, the release induced by *C. albicans* was fairly marked. Basophils from patients under 30 years of age at onset were reactive to house dust and anti-IgE, while the cells from patients over 41 years of age at onset tended to be reactive only to *C. albicans*. Basophils from patients with low serum IgE levels were less reactive than the cells from patients with high levels of IgE to house dust and anti-IgE. *C. albicans*-induced release of histamine did not correlate with serum IgE levels.

KEYWORDS: histamine release, blood basophils, specific allergen, anti-IgE, IgE receptors

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COMPARISON OF BASOPHIL HISTAMINE RELEASE INDUCED BY THE CROSS-LINKING OF IgE RECEPTORS

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Abstract. Basophil histamine release induced by allergens (house dust and *Candida albicans*) and anti-IgE was examined in 31 patients with bronchial asthma in relation to patient age, age at onset of the disease and serum IgE levels. Basophils from patients under 40 years of age generally released a significantly large amount of histamine by stimulation with house dust and anti-IgE. On the other hand, histamine release from patients over 41 years of age was generally not marked when the cells were incubated with house dust and anti-IgE, although, in some cases, the release induced by *C. albicans* was fairly marked. Basophils from patients under 30 years of age at onset were reactive to house dust and anti-IgE, while the cells from patients over 41 years of age at onset tended to be reactive only to *C. albicans*. Basophils from patients with low serum IgE levels were less reactive than the cells from patients with high levels of IgE to house dust and anti-IgE. *C. albicans*-induced release of histamine did not correlate with serum IgE levels.

Key words : histamine release, blood basophils, specific allergen, anti-IgE, IgE receptors.

Basophil histamine release induced by specific allergens and anti-IgE has been extensively studied (1-6). The mechanism of IgE-mediated histamine release from basophils is thought to be essentially identical to allergen-mediated release, although some differences in the release mechanism are observed between specific allergens and anti-IgE (5). House dust is one of the main allergens eliciting bronchial asthma. The allergen acts on basophils through the cross-linking of IgE receptors. Our previous studies have shown that histamine release from basophils induced by house dust parallels the release caused by anti-IgE in patients sensitive to the allergen. *Candida albicans* is also one of the main allergens causing asthma and induces histamine release from basophils through the cross-linking of IgE receptors (7).

In this study, basophils from the same donors were challenged by house dust, *C. albicans* and anti-IgE, and the amount of histamine released was compared among them in relation to patient age, age at onset of the disease and serum IgE levels.

SUBJECTS AND METHODS

Subjects. Thirty-one patients with bronchial asthma (20 females and 11 males) were selected for this study. Their ages ranged from 19 to 72 years with a mean of 46.3 years. The mean age at onset of the disease was 31.2 years (4-71), and the mean serum IgE level was 683 IU/ml (45-2840). They showed a positive skin reaction to house dust and/or *C. albicans*.

Histamine release. The release of histamine from basophils after addition of the specific allergens (house dust and *C. albicans*) and anti-IgE was examined using a whole blood method, as previously described (8, 9). To 4 ml of heparinized venous blood, 0.2 ml of a ten-fold dilution of house dust (2.9 mcgPN/ml, Torii Co.), *C. albicans* (0.16 mcgPN/ml, Torii Co.) or anti-IgE (Hoechst) was added. After the mixed solution was incubated at 37 °C for 15 min, the reaction was stopped by transferring the test tube to an ice bath. The histamine content of the cells and supernatant fluid was measured by an automated spectrofluorometric histamine analysis system (Technicon). The results were expressed as the percentage of histamine release.

Serum IgE levels. Serum levels of total IgE was measured by a radioimmunosorbent test (RIST ; Pharmacia).

RESULTS

Histamine release and patient age. The mean percent histamine release from basophils induced by house dust was high in patients aged between 0 and 30 years ($33.9 \pm 7.6\%$) (mean \pm SE), and between 31 and 40 years ($32.7 \pm 9.0\%$). The degree of house dust-induced release of histamine was low in patients aged between 41 and 50 years ($10.8 \pm 7.0\%$) and over 51 years ($13.5 \pm 3.7\%$). A significant difference in histamine release induced by house dust was found between patients aged 0-30 and those over 51 years ($p < 0.02$). Basophil histamine release induced by anti-IgE showed almost the same tendency as the house dust-induced release. The results demonstrate that histamine release induced by house dust and anti-IgE become less marked with aging. The release of histamine caused by *C. albicans* did not correlate with patient age. As shown in Fig. 1, basophils of the two patients between the ages of 0 and 30 released a significant amount of histamine by all three stimulating agents. However, basophils of the three patients over 51 years of age released a large amount of histamine by stimulation with *C. albicans*, while the release of histamine induced by house dust and anti-IgE was not marked in these three patients (Fig. 1).

Histamine release and age at onset. Basophils of patients between 21 and 30 years of age at onset released a large amount of histamine by stimulation with house dust ($45.1 \pm 5.9\%$) and anti-IgE ($46.1 \pm 6.0\%$). The release by either agent was not marked in patients over 41 years of age at onset (house dust, $8.4 \pm 2.1\%$; anti-IgE, $17.7 \pm 3.1\%$). The results demonstrate that the release of histamine induced by house dust and anti-IgE was marked in cases under 40 years of age at onset. The mean of *C. albicans*-induced histamine release was lowest ($7.0 \pm 1.7\%$) in patients under 20 years of age at onset and highest ($24.4 \pm 7.0\%$) in patients over 41 years of age at onset. The degree of histamine release induced by *C. albicans* was significantly higher in the latter cases than in the former cases ($p < 0.05$) (Fig. 2).

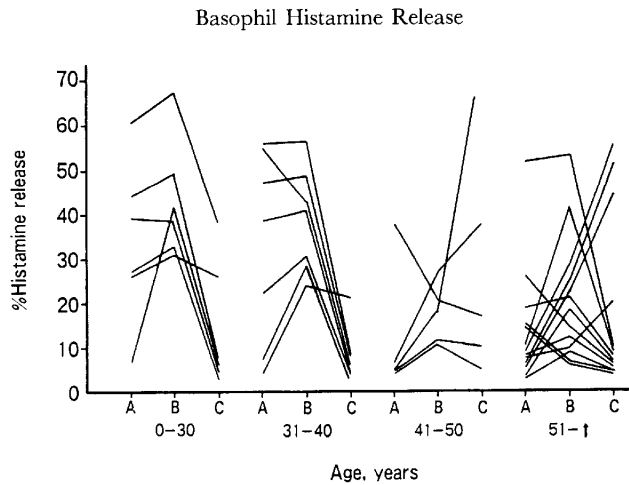


Fig. 1. Histamine release from basophils of asthmatics induced by house dust, *Candida albicans* and anti-IgE in relation to patient age. A : house dust, B : anti-IgE, C : *Candida albicans*

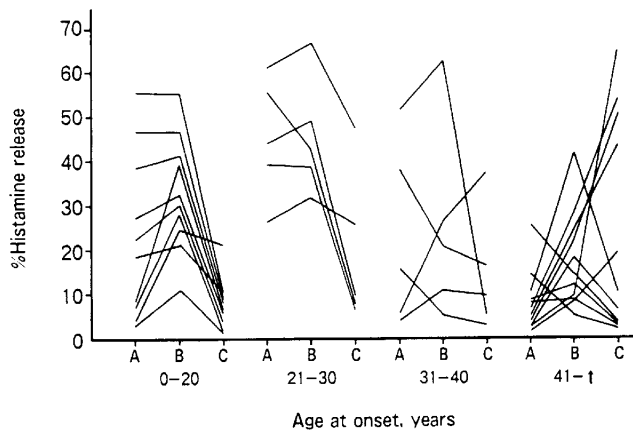


Fig. 2. Histamine release from basophils of asthmatics induced by house dust, *Candida albicans* and anti-IgE in relation to age at onset. A : house dust, B : anti-IgE, C : *Candida albicans*

Histamine release and serum IgE levels. Histamine release induced by house dust and anti-IgE tended to increase with higher serum IgE levels. The release induced by anti-IgE was significantly more marked in patients with serum IgE levels higher than 1001 IU/ml ($41.6 \pm 8.4\%$) than in patients with levels ranging from 0 to 300 IU/ml ($21.5 \pm 4.1\%$) ($p < 0.05$). There was no correlation between *C. albicans*-induced histamine release and serum IgE levels. In cases showing a significant histamine release reaction to *C. albicans*, basophils were less reactive to house dust and anti-IgE when their serum IgE levels were low (0-300 IU/ml). However, they were more reactive to both agents when the IgE levels were high (more than 1001 IU/ml) (Fig. 3). The results suggest that serum IgE levels affect the reactivity

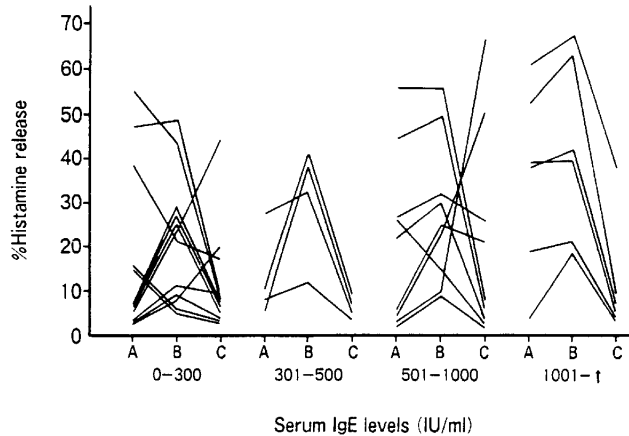


Fig. 3. Histamine release from basophils of asthmatics induced by house dust, *Candida albicans* and anti-IgE in relation to serum IgE levels. A : house dust, B : anti-IgE, C : *Candida albicans*

of basophils through the cross-linking of IgE receptors, and that basophil reactivity to allergens and anti-IgE increases with higher serum IgE levels.

DISCUSSION

Basophil reactivity to specific allergens and anti-IgE can be observed by morphological changes (10-12) and by estimating the release of chemical mediators. Among the chemical mediators released from basophils, histamine has been the most frequently examined. It has been suggested that there are some differences in dose-response curves for histamine release between specific allergens and anti-IgE (5). However, no difference is found between specific allergens and anti-IgE when the results are expressed as the maximum percent of histamine release. In fact, a good correlation was found between the maximum percent of histamine release induced by house dust and anti-IgE ($r = 0.75$, $p < 0.001$) (13).

The reactivity of basophils varies depending on the pathogenesis of asthma (14). In the present study, basophil reactivity to house dust, *C. albicans* and anti-IgE was examined in patients with bronchial asthma in relation to patient age, age at onset and serum IgE levels. The results obtained here suggest that these factors affect basophil reactivity to allergens and anti-IgE. The reactivity of basophils was generally high in patients under 40 years of age, in patients under 30 years of age at onset and in patients with high serum IgE levels (more than 1001 IU/ml). Basophils of these patients release a large amount of histamine upon exposure to house dust, *C. albicans* and anti-IgE. On the other hand, the reactivity of basophils was generally low in patients over 41 years of age, in patients over 41 years of age at onset and in patients with low serum IgE levels (less than 300 IU/ml). Basophils of these patients were generally less reactive to house dust, *C. albicans* and anti-IgE

than the cells of the younger patients and patients with high serum IgE levels, although the cells of same patients were more reactive to *C. albicans*. These results suggest that the IgE-mediated response of basophils becomes less marked with aging, and that the selectivity of basophil reaction to *C. albicans* is due to increased levels of specific IgE antibodies which are frequently observed in patients over 41 years of age (15).

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